

A molecular signature of lung and CLL cancers: Novel biomarker proteins for diagnosis, prognosis and treatment

Varda Shoshan Barmatz, Ann Shteinfer Kuzmine, Yael Bishitz Y, Paul A and Krelin Y NIBN- Ben-Gurion University of the Negev, Israel

ancers cells undergo re-programing of metabolism, cell survival and anti-apoptotic defenses, with the proteins mediating these re-programing representing potential biomarkers. Here, using specific antibodies, mass spectrometry and bioinformatics tools; we searched for novel biomarker proteins in chronic lymphocytic leukemia (CLL) and in non-small cell lung cancer (NSCLC) patient samples that can impact diagnosis, treatment and prognosis. By comparing protein expression profiles of CLL- and healthy donor-derived lymphocytes, we identified 1,360 differentially expressed proteins, some shown for the first time to be associated CLL. Down-regulated expression of two proteins resulted in cell growth inhibition, pointing to their essential functions. Based on changes in the levels of several proteins in CLL patients, we could distinguish between patients in a stable disease state and those

who would be later subjected to anti-cancer treatments, 2-3 years before the physician's decision. In NSCLC, the adenocarcinoma (AC) and squamous cell carcinoma (SCC), sub-types present unique genomes, transcriptomes, and proteomes, and share clinical and histopathological characteristics, yet differ in treatment. We identified novel biomarker proteins in NSCLC, with 378 proteins showing a $\geq |100|$ -fold change in level. Several, identified for the first time, allow for distinguishing between AC and SCC. These, together with markers previously proposed and confirmed here, lead us to propose a list of proteins for discriminating SCC and AC, with four being secreted. Precise diagnosis of AC and SCC is essential for selecting appropriate treatment. Finally, some of these biomarkers can serve as new targets and lead to new treatments for lung and CLL cancers.

vardasb@bgu.ac.il

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